REMARKS

In the instant Action, claims 1-22, 26, 30-34 and 38 are listed as pending and all claims are rejected. Claim 2 is currently amended to incorporate the limitations of claim 1, from which it originally depended. Support for this amendment may be found in the claims as originally filed. Claim 20 previously was dependent upon claim 1 and is now amended to depend from claim 2. Claims 30 and 38 are currently amended to depend from claim 2. Support for this amendment may be found in the specification at page 24 lines 10-13 and page 27, lines 4-14, respectively. Claim 33 is amended to conform to amendments made to claim 30, from which claim 33 depends. Claims 18, 19 and 21 are amended to correct typographical errors in the term "anthracyclin", correcting the term to read "anthracycline". Support for this correction can be found throughout the specification, for example at page 7 lines 20-25. Applicants submit that the amendments do not introduce new matter.

Claim 1 is canceled in this reply. Claims 23-25, 27-29, 35-37 and 39-40 were previously canceled. Applicant expressly reserves the right to reclaim the canceled subject matter in a subsequent application.

Applicants are grateful for entry of the Preliminary Amendments of March 25, 2005 and for the Examiner's consideration of the Information Disclosure Statement submitted on April 21, 2005.

CLAIM REJECTIONS

1. Claim Rejections – 35 U.S.C. § 112, First Paragraph

1A. Rejection of claims 1, 20, 30-33 and 38 under 35 U.S.C. 112, first paragraph

On pages 2-6 of the instant Action, the Examiner has rejected claims 1, 20, 30-33 and 38 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner alleges that the specification, while being enabling for a pharmaceutical composition comprising a farnesyl transferase inhibitor of Formula I and an anthracycline, does not

reasonably provide enablement for any farnesyl transferase inhibitor or prodrug thereof and an anthracycline or prodrug thereof. The complete details of the Examiner's comments are found on pages on pages 2-6 of the instant Action and are not reiterated in full in this reply.

1B. Amendments to the claims

Applicants note that instant claims 2, 18-21, 30, 33 and 38 have been amended. Claim 1 has been canceled.

1C. Claims 1, 20, 30-33 and 38 do not violate 35 U.S.C. 112, first paragraph

Without conceding to the correctness of the Examiner's allegations, and solely in an effort to advance the prosecution of the instant application, Applicants have canceled claim 1 and amended claims 20, 30 and 38. Applicants submit that the cancellation of instant claim 1 renders moot this rejection against said claim.

Applicants note that instant claims 20, 30 and 38 now depend from claim 2, which has been amended to recite a pharmaceutical composition comprising the particular farnesyl transferase inhibitors of Formula I and an anthracycline. Claims 31-33 depend from claim 30 and thus now incorporate the new limitations of claim 30. Applicants submit that the instant claims are fully enabled by the specification for a pharmaceutical composition comprising a farnesyl transferase inhibitor of Formula I and an anthracycline.

1D. Request for withdrawal of rejection of claims 1, 30-33 and 38 under 35 U.S.C. § 112, first paragraph

Applicants submit that, for the amendments and reasons cited above, claims 20, 30-33 and 38 are fully enabled. Applicants request the reconsideration and withdrawal of the rejection of claims 20, 30-33 and 38 under 35 U.S.C. § 112, first paragraph.

2. Claim Rejections – 35 U.S.C. § 112, First Paragraph

2A. Rejection of claims 1-17, 20-22 and 26 under 35 U.S.C. 112, first paragraph

On pages 6-9 of the instant Action, the Examiner has rejected claims 1-17, 20-22 and 26 under 35 U.S.C. § 112, first paragraph for lack of enablement. The Examiner

alleges that the specification, while being enabling for compositions comprising the disclosed active agents and method comprising administering said compositions, does not reasonable provide enablement for compositions comprising a "prodrug" component(s). The complete details of the Examiner's comments are found on pages on pages 6-9 of the instant Action and are not reiterated in full in this reply.

2B. Amendments to the claims

Claim amendments are as previously described.

2C. Claims 1-17, 20-22 and 26 do not violate 35 U.S.C. 112, first paragraph

Without conceding to the correctness of the Examiner's allegations, and solely in an effort to advance the prosecution of the instant application, Applicants have canceled claim 1 and amended claim 20 to delete the offending term "prodrug".

2D. Request for withdrawal of rejection of claims 1-17, 20-22 and 26 under 35 U.S.C. § 112, first paragraph

Applicants submit that, for reasons cited above, the method of claim 2-17 and claims 20-22 and 26 are fully enabled by the specification for compositions comprising the disclosed farnesyl transferase inhibitor and anthracycline compositions and methods comprising administering said compositions. Applicants request the reconsideration and withdrawal the rejection of claims 1-17, 20-22 and 26 under 35 U.S.C. § 112, first paragraph.

3. Claim Rejections – 35 U.S.C. § 103(a)

3A. Rejection of claims 1-22, 26, 30-34 and 38 under 35 U.S.C. 103(a)

On pages 10-12 of the instant Action, the Examiner has rejected claims 1-22, 26, 30-34 and 38 under 35 U.S.C. § 103(a) as being unpatentable over Gordon *et al.* (PCT International Publication WO 00/39130, referred to hereinafter as "Gordon") in light of Rybak (PCT International Publication WO 01/64197, referred to hereinafter as "Rybak"). In brief, the Examiner alleges that as Gordon discloses the farnesyl transferases of instant claims 2 and 3-17, and as Rybak discloses therapeutic combinations of anthracyclines and farnesyl transferase inhibitors, it would have been obvious to the

skilled artisan to provide a pharmaceutical composition comprising a farnesyl transferase inhibitor according to Gordon and an anthracycline such as doxorubicin. The Examiner further alleges that as farnesyl transferase inhibitors and anthracyclines are believed to exhibit anti-tumor activity, it would be obvious to use a combination of farnesyl transferase inhibitors and anthracyclines to treat nasopharyngeal carcinoma. The complete details of the Examiner's comments are found on pages on pages 10-12 of the instant Action and are not reiterated in full in this reply.

3B. Amendments to the claims

Claim amendments are as previously described.

3C. Claims 1-22, 26, 30-34 and 38 are not obvious over Gordon in light of Rybak

Applicants respectfully disagree that the claimed invention is obvious over Gordon in light of Rybak. Applicants submit that the Examiner has failed to meet the basic CAFC requirement that an obviousness rejection be supported by some suggestion in the prior art to create the claimed invention:

> [A] proper analysis under §103 requires, *inter alia*, consideration of . . . whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed invention,

In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991) (emphasis added).

Firstly, the Examiner alleges that the Rybak reference teaches the skilled artisan to combine anthracyclines with the farnesyl transferase inhibitors of Gordon to produce the claimed compositions of the instant invention. Applicants respectfully disagree. Applicants respectfully submit that Gordon makes no reference to the combination of farnesyl transferase inhibitors with anthracyclines at all, and Rybak is silent as to the use of any other farnesyl transferase molecules in combination with anthracyclines except for those recited in Rybak (see Rybak page 13 lines 2-10, in which Rybak specifies "a farnesyl transferase inhibitor of the type described above" (line 4) and "a farnesyl transferase inhibitor of formula (I), (II), (III), (IV), (V), (VI), (VII), (VII) or (IX) above, in particular a compound of formula (I), (II) or (III)". Applicants thus respectfully submit

that neither Gordon nor Rybak teach or suggest the idea of a pharmaceutical composition comprising Applicants' *particular* farnesyl transferase inhibitors in combination with anthracyclines.

Secondly, the Examiner alleges that the combination of Rybak and Gordon teach the skilled artisan to combine anthracyclines with farnesyl transferase inhibitors to treat nasopharyngeal carcinoma. Applicants respectfully disagree. Applicants submit that neither Gordon nor Rybak make reference to nasopharyngeal carcinoma, thus the combination fails to teach or suggest the idea of treating nasopharyngeal carcinoma using Applicants' claimed compositions.

As further detailed by the CAFC a "proper obviousness analysis requires consideration of whether the prior art would also have revealed that in so making or carrying out [the claimed invention], those of ordinary skill would have a reasonable expectation of success." *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). In light of the arguments presented herein, Applicants respectfully submit that Rybak fails to demonstrate that a combination of a farnesyl transferase inhibitor and an anthracycline actually confers an anti-tumor effect. Absent a demonstration of efficacy, Applicants submit that Rybak, combined with Gordon, fails to lead the skilled artisan to reasonably expect that the two compounds would function in concert to have an effect.

In contrast, Applicants have elegantly shown that doxorubicin in combination with farnesyl transferase inhibitor Compound A results in a greater decrease in cell viability as compared to doxorubicin or Compound A alone (see instant Figure 1). The compounds together also exhibit an increase in the induction of caspase activity (see instant Figure 4), in PARP cleavage (see instant Figure 5), and in the induction of Traf 1 cleavage (see instant Figure 6).

Applicants further submit that the Examiner has failed to support his conclusion that two compounds allegedly "known to be useful for the treatment of cancer broadly" can also be used to treat a particular subset of cancer, such as nasopharyngeal carcinoma. As explained by Applicants in the specification at page 1 line 1 continuing through to page 4 line 29, nasopharyngeal carcinoma is a rather unique cancer

characterized by the consistent association with Epstein Barr Virus, involvement of p16/INK4 and difficulty to culture *in vitro*. Applicants submit that the skilled cancer researcher would be aware that different cancers exhibit unique gene expression patterns, *e.g.* BRCA1 is often expressed in breast cancer and c-myc is often disrupted in Burkitt's lymphoma, and often require different treatments. The Examiner has failed to provide any reference teaching that a farnesyl transferase inhibitor in combination with anthracycline purported for use against a non-nasopharyngeal cancer would be efficacious against nasopharyngeal cancer. Absent such a teaching, and absent any data in Rybak demonstrating an actual anti-tumor effect of a farnesyl transferase inhibitor in combination with anthracycline, Applicants respectfully submit the combination of Gordon and Rybak cannot and does not lead the skilled artisan to expect successful treatment of nasopharyngeal carcinoma utilizing a combination of farnesyl transferase inhibitor and anthracycline.

In summary, Applicants submit that the Examiner has failed to meet both the "should make the claimed invention" as well as "expectation of success" prongs of the obviousness requirement.

On pages 11-12 of the instant Action, the Examiner rejects claims 34 and 38 directed to kits comprising the pharmaceutical compositions of the invention as being obvious and within the knowledge and skills of the pharmacologist. The Examiner further notes that the U.S. Court of Appeals recently ruled that "a kit *of the prior art* with a set of instructions" is unpatentable (see In re Ngai 03-1524; emphasis added). Applicants respectfully submit that as the combination of farnesyl transferase inhibitor compounds according to Formula I in combination with anthracycline compounds is a novel and non-obvious combination, a kit derived with such compounds and compositions is also a novel and non-obvious invention.

3D. Request for withdrawal of rejection of claims 1-22, 26, 30-34 and 38 under 35 U.S.C. § 103(a)

Applicants submit that, for reasons cited above, claims 1-22, 26, 30-34 and 38 are in no way made obvious by Gordon in light of Rybak. Applicants request the

reconsideration and withdrawal the rejection of claims 1-22, 26, 30-34 and 38 under 35 U.S.C. § 103(a).

Reconsideration of the instant Office Action, entry of the amendments submitted herewith, and allowance of all pending claims are respectfully requested. Prompt and favorable action is solicited.

Respectfully submitted,

Date:
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